Specifications

The Examiner has objected to claims 11-14, reciting distinct donor species as lacking antecedent basis in the specification. The Examiner cites page 9, line 25 - page 10, line 8 as disclosing donor/acceptor pairs not distinct donor species. Applicants respectfully direct the Examiner's attention to lines 1 and 4 on page 10 which refers to multiplexing of donor/acceptor pairs. Multiplexing may be accomplished by using multiple donors with the same acceptor. It does not require that both members of the pair are different. The specification is directed toward use of APC as the acceptor, and does not disclose other acceptors; therefore it is implicit that the donor must be varied to achieve multiplexing. Applicants respectfully direct the Examiner to page 10, lines 9-11 which disclose preferred donor species. These are specific chemical entities which are not disclosed as a part of a donor/acceptor pair, but as a list of discreet chemical entities that may be used with APC to achieve multiplexing. Further Applicants have amended the specification at page 4 after line 21 to include a paraphrase of original claim 11-14 which should further clarify the use of the phrase "distinct donor species." As this is matter included in the claims as filed, it does not add new matter. Accordingly, Applicants assert that the specification does support the "distinct donor species" claimed in claims 11-14 and respectfully request that the Examiner withdraw the objection to the use of "distinct donor species" in the claim.

As indicated in the Specification amendments above, Applicants have corrected page 19, line 4 of the specification to read "Figure 5", not Figure 6. This corrects a clerical error and adds no new matter.

Rejections Maintained

Claim Definitions - 35 U.S.C. § 112

The Examiner has rejected claims 3-14 under 35 U.S.C. § 112, first paragraph as assertedly being enabling for 1 M sodium perchlorate but not providing enablement for any and all gentle chaotropic agents.

Applicants assert that the relative strength of chaotropic agents is well known in the art. For example, the textbook Food Chemistry 3rd Edition edited by Owen R. Fennema devotes Chapter 6 to a basic general discussion of protein chemistry. A section on "Chaotropic Salts and Denaturation" is included on page 364 of that chapter. The first paragraph of this section ends with the statements "The relative ability of various anions at isotonic strength to influence the structural stability of protein (and DNA) in general follows the series $F^- < SO_4^{2-} < C_l^- < B_R^- < I^- < ClO_4^- < SCN^- < Cl_3CCOO^-$. This ranking is known as the Hofmeister series or "chaotropic series."

Thus, the Applicants submit that chaotropic agents and relative strength of chaotropic agents is well known and accessible to one skilled in the art of protein science. Accordingly, Applicants' provision of the bench mark of 1 M sodium perchlorate is sufficient for one skilled in the art to select other gentle chaotropic agents without undue experimentation. One skilled in the art could apply the known Hofmeister series in conjunction with Applicants' disclosure to ascertain other suitable gentle agents and/or eliminate unsuitable agents without undue experimentation. The disclosed criteria of the treatment with gentle chaotropic agent not affecting the final 650/620 and 650/280 nm ratio of the cross-linked allophycocyanin as described in the specification serves as a straightforward, readily performable test to confirm the desired result. Thus, one skilled in the art can readily ascertain that he has prepared the disclosed

composition without undue experimentation. The combination of the Hofmeister series, which is well known in the art, Applicants' example and Applicants' criteria for measuring the absorbency ratios of the cross-linked product at specified wave lengths is ample information for one skilled in the art to apply the Applicants' procedure beyond the specifically disclosed perchlorate example. Accordingly, Applicants' request that the Examiner withdraw the rejection of claims 3-14 under 35 U.S.C. § 112.

The Examiner has rejected claims 3-14 under 35 U.S.C. § 112, second paragraph, as being indefinite for the recitation of "having the ability" in claim 3. Without conceding that amendment is necessary, Applicants have amended Claim 3 to remove this phrase. Accordingly, applicants' request that the Examiner withdraw the rejection of claims 3-14 under 35 U.S.C. § 112 second paragraph.

Claim Rejection - 35 U.S.C. § 103

Applicants note Examiner's comments regarding the obligation to comply with 37 C.F.R. 1.56 and indicate that at the time of invention all the inventors had an obligation to assign the invention to the current assignee.

The Examiner has rejected claims 3-10 under 35 U.S.C. § 103(a) as being unpatentable over Park et al. in view of Applicants' statement regarding Applicant's sale of product in IDS filing December 3, 2003. Applicants respectfully traverse the rejection.

Park describes a method for a Tyrosine Kinase Assay which discloses quantitating an analyte by measuring time resolved transfer of fluorescence energy to or from a labeled quantity, including the use of donor compounds to absorb light energy and the transfer of this absorbed energy to cross-linked allophycocyanin. Use of cross-linked allophycocyanin which has not been exposed to strongly chaotropic agents, in the methods of Park is not obvious for at least the

following reasons. First, the Applicants claim an "improvement" to methods for quantitating analyte using time resolved transfer of fluorescent energy. Accordingly, Applicants are not arguing whether such assays existed prior to their invention but rather that their invention provides a significant and patentable improvement over the known assays. Further, at the time of Applicants' first sale of the cross-linked allophycocyanin that had not been exposed to strongly chaotropic agents, it was not known nor was there any expectation that cross-linked allophycocyanin which had not been exposed to strongly chaotropic agents had any particular technical benefits when used in assays. The modified preparation procedure for the cross-linked allophycocyanin was adopted to facilitate manufacture without affecting fluorescent properties.

Thus, there was no expectation that combining the Applicants' product with known methods, such as the method of Park, would yield any change in fluorescent properties and/or an improved assay. Applicants accidentally and unexpectedly discovered substantially after the sale of their product that use of cross-linked allophycocyanin not exposed to strong chaotropic agents in the analyses such as those described in Applicant's specification yielded significantly improved analytical results including substantially improved sensitivity.

Applicants direct the Examiner to Example 8 which begins on page 16, line 23 of the Specification. This example describes comparison of SL-APC and XL-APC streptavidin conjugates in two different kinase assays. Data from the comparisons described in Example 8 is provided in Figure 4 (corrected figure number). As the data of Figure 4 shows, SL-APC streptavidin conjugate of the invention in TR-FRET for src kinase assay demonstrated an improved sensitivity over commercially available XL-APC streptavidin. The non-obviousness of Applicants' invention is further emphasized by the fact that experimentation was required to

establish the fact that the cross-link allophycocyanin which had not been exposed to strongly chaotropic agents was indeed related to the improved analytical results.

Thus prior to the inventor's unexpected discovery there was no expectation that Park in combination with Applicants' product would provide an improved assay.

The Examiner has also rejected claim 11-14 under 35 U.S.C. § 103(a) as unpatentable over Park et al. and Applicants' sale of cross-linked allophycocyanin which had not been exposed to strongly chaotropic agents. Again, as described in detail above, prior to Applicants' discovery there was no expectation that Applicants' product could provide any change in fluorescent properties and/or an improved assay and hence no expectation that combination of the Applicants' product in an assay of the type described by Parks would yield a result of the type discovered by Applicants.

Accordingly Applicants request that the Examiner withdraw the rejection of claims 3-10 and 11-14 under 35 U.S.C. 103(a).

Examiner's Response to Arguments

Applicants acknowledge the Examiner's Response to Arguments on page 9 of the office action and thank the Examiner for withdrawing the previous rejection of claims 3-6, 9 and 10 under 35 U.S.C. § 103 over Park in view of Ong. As to the Examiner's further comments on the use of the phrase "having the ability" in claim 3. Applicants believe that the amendment of Claim 3 provided and discussed above, which does not change the scope of the claim, will resolve this issue.

CONCLUSION

For at least the reasons set forth above, Applicants respectfully submit that claims 3-14 are in condition for allowance. Applicants therefore request that the claims be allowed.

Respectfully submitted,

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